ATTORNEY DOCKET NO. 14028.0293U1 APPLICATION NO. 09/869,869

Listing of Claims

- 1. (Currently Amended) A method of preventing chronic rejection of a transplant in a recipient comprising:
 - (a) administering to the recipient a <u>an anti-CD3</u> immunotoxin, thereby reducing the recipient's T-cell population; and
 - (b) administering to the recipient a costimulation blocker, thereby reducing a transplant-specific antibody response.
- 2. (Original) The method of claim 1, wherein the transplant is allogeneic.
- 3. (Original) The method of claim 1, wherein the recipient is a mammal.
- 4. (Original) The method of claim 3, wherein the mammal is a primate.
- 5. (Original) The method of claim 4, wherein the primate is a human.
- 6. (Original) The method of claim1, wherein the immunotoxin transiently reduces the subject's T cells in the blood and lymph nodes by at least one log unit.
- 7. (Currently amended) The method of claim 1, wherein the immunotoxin is a divalent anti-T cell immunotoxin directed at the CD3 epitope.
- 8. (Currently Amended) The method of claim 7, wherein the divalent anti-T cell immunotoxin comprises a toxin moiety and a targeting moiety directed to the T cell CD3ɛ epitope.
- 9. (Original) The method of claim 8, wherein the toxin moiety is a diphtheria toxin.
- 10. (Currently Amended) The method of claim 9, wherein the divalent anti-T cell immunotoxin is UCHT1-CRM9.
- 11. (Original) The method of claim 1, wherein the transplant is derived from a living donor.

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- 12. (Original) The method of claim 1, wherein the transplant is derived from a cadaveric donor.
- 13. (Original) The method of claim1, wherein the transplant is selected from the group consisting of kidney, liver, heart, pancreas, lung, and skin transplants.
- 14. (Original) The method of claim 1, wherein the costimulation blocker blocks the CD40:CD154 pathway.
- 15. (Original) The method of claim 14, wherein the blocker of the CD40: CD154 pathway is an anti-CD154.
- 16. (Original) The method of claim 15, wherein the anti-CD154 is 5C8.
- 17. (Original) The method of claim 14, further comprising administering a second costimulation blocker, thereby further reducing the transplant-specific antibody response.
- 18. (Original) The method of claim 17, wherein the second costimulation blocker blocks the B7: CD28 pathway.
- 19. (Original) The method of claim 18, wherein the blocker of the B7: CD28 pathway binds to B7 and blocks binding B7 with CD28.
- 20. (Original) The method of claim 19, wherein the blocker of the B7: CD28 pathway is CTLA 4-Ig.
- 21. (Original) The method of claim 1, wherein the costimulation blocker blocks the B7: CD28 pathway.
- 22. (Original) The method of claim 21, wherein the blocker of the B7: CD28 pathway is CTLA4-Ig.
- 23. (Original) The method of claim 1, wherein the immunotoxin is administered at least three times.

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- 24. (Original) The method of claim 23, wherein the immunotoxin is administered at least on the day of transplanting and on two days immediately following transplanting.
- 25. (Original) The method of claim1, wherein the costimulation blocker is administered at least once.
- 26. (Original) The method of claim 25, wherein the costimulation blocker is administered at least on the day of transplanting and on three additional days within the first week following transplanting.
- 27. (Original) The method of claim 1, further comprising administering an immunosuppressive agent to the recipient.
- 28. (Original) The method of claim 27, wherein the immunosuppressive agent is selected from the group consisting of cyclosporine, mycophenolate moefitil, tacrolimus, azathioprine, and steroid and any combination thereof.
- 29. (Original) A method of reversing a late acute rejection of an transplant by a recipient having a transplant that has survived for a prolonged period of time using the method of claim 1, comprising:
 - (a) monitoring the recipient for an indicator of a late acute rejection; and
 - (b) administering to the recipient showing the indicator of the late acute rejection an immunotoxin, thereby reducing the recipient's T-cell population.
- 30. (Original) The method of claim 29, wherein the transplant is selected from the group consisting of kidney, liver, heart, pancreas, lung, and skin transplants.
- 31. (Original) The method of claim 30, wherein the indicator of the acute rejection response of the kidney transplant is elevated serum creatinine.
- 32. (Original) The method of claim30, wherein the indicator of the acute rejection response of the kidney transplant is a histologic indicator.
- 33. (Original) The method of claim 32, wherein the histologic indicator is tubulitis.